510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k053079

B. Purpose for Submission:

Premarket notification (510k) of the intent to manufacture and market the Assure Pro Blood Glucose Monitoring system.

C. Measurand:

Capillary blood glucose

D. Type of Test:

Quantitative enzymatic (glucose oxidase) electrochemical assay

E. Applicant:

Hypoguard USA, Inc.

F. Proprietary and Established Names:

Assure Pro Glucose Monitoring System

G. Regulatory Information:

1. Regulation section:

   21 CFR §862.1345, Blood Glucose Test System, Over-the-Counter
   21 CFR §862.1660 Quality control material (assayed and unassayed)

2. Classification:

   Class II

3. Product code:

   CGA, NBW, JJX

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   Please see indications for use.

2. Indication(s) for use:

   Assure Pro Blood Glucose Monitoring System:
   The Assure Pro Blood Glucose Meter is intended for the quantitative measurement of glucose in fresh capillary whole blood. Testing is done outside the body (In Vitro Diagnostic Use). It is indicated for use at home (over the counter [OTC]) by persons with diabetes, or in clinical settings by healthcare professionals, as an aid to monitor the effectiveness of diabetes control.

   Assure Pro Glucose Meter:
   The Assure Pro Blood Glucose Meter is intended for the quantitative measurement of glucose in fresh capillary whole blood. Testing is done outside the body (In Vitro Diagnostic Use). It is indicated for use at home (over the counter [OTC]) by persons with diabetes, or in clinical settings by healthcare professionals, as an aid to monitor the effectiveness of diabetes control.

   Assure Pro Blood Glucose Test Strips:
   Assure Pro Test Strips are intended for the quantitative measurement of glucose in fresh capillary whole blood when used with the Assure Pro Blood Glucose Meter. Testing is done outside the body (In Vitro Diagnostic Use). It is indicated for use at home (over the counter [OTC]) by persons with diabetes, or in clinical settings by healthcare professionals, as an aid to monitor the effectiveness of diabetes control.

   Assure Pro Control Solution:
   For use with Assure Pro Blood Glucose and Assure Pro Test Strips as a quality control check to verify the accuracy of blood glucose test results.

3. Special conditions for use statement(s):

   For use with capillary whole blood (fingerstick only).

4. Special instrument requirements:

   None – the Assure Pro is a complete blood glucose monitoring system.

I. Device Description:

The Assure Pro Blood Glucose Monitoring System consists of a meter, test strips, and control solutions (two levels). It is intended for over-the-counter, home use by diabetics to monitor their blood glucose levels, of for use in a clinical setting by health care professionals. The system tests fresh capillary whole blood. The meter is a portable, battery-operated instrument designed for use with Assure Pro Blood Glucose test strips.

The device uses well established biochemical, electrical, and software methodologies to report plasma equivalent glucose concentrations from fingerstick sampled capillary whole blood. No new or unproven techniques are introduced with this device. The Assure Pro Blood Glucose Monitoring System can measure glucose concentrations ranging from 20 to 600 mg/dL in whole capillary blood with hematocrits ranging from 30-55%

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Assure Pro Blood Glucose Monitoring System

2. Predicate 510(k) number(s):

   k051514

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Analyte	Glucose	Same
Enzyme	Glucose Oxidase	Same
Measurement Method	Electrochemical	Same
Calibration	Strip specific on a disposable chip	Same
Matrix	Fingerstick whole blood	Same

Differences		
Item	Device	Predicate
Measurement Time	10 seconds	15 seconds
Applied Volume	1 uL	1.5 uL

K. Standard/Guidance Document Referenced (if applicable):

FDA Guidance Document: Review Criteria for Assessment of Portable Blood Glucose In Vitro Diagnostic Devices Using Glucose Oxidase, Dehydrogenase, or Hexokinase Methodology

CLSI EP05-A2: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline-Second Edition

CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline- Second Edition

ISO 15197: Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus

L. Test Principle:

The test is based on the release of electrical potential after a two-step reaction where glucose and ferricyanide, in the presence of glucose oxidase, are converted into gluconolactone and ferrocyanide. Ferrocyanide, when electrical current is applied, becomes ferricyanide and releases electrons; the increase in current measured by the meter is proportional to the glucose concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The company followed ISO 15197 in quantifying the precision of their glucose system. The company made measurements on pooled venous blood spiked to 5 different glucose concentrations on 10 different meters using strips from 10 different vials taken from one manufacturing lot for a total of 100 measurements per glucose concentration, 500 measurements per manufacturing lot. The company repeated this procedure on 3 different production lots for a total of 1500 measurements. Five values were excluded when the meter produced no result because of technician error.

A summary of the company's findings:

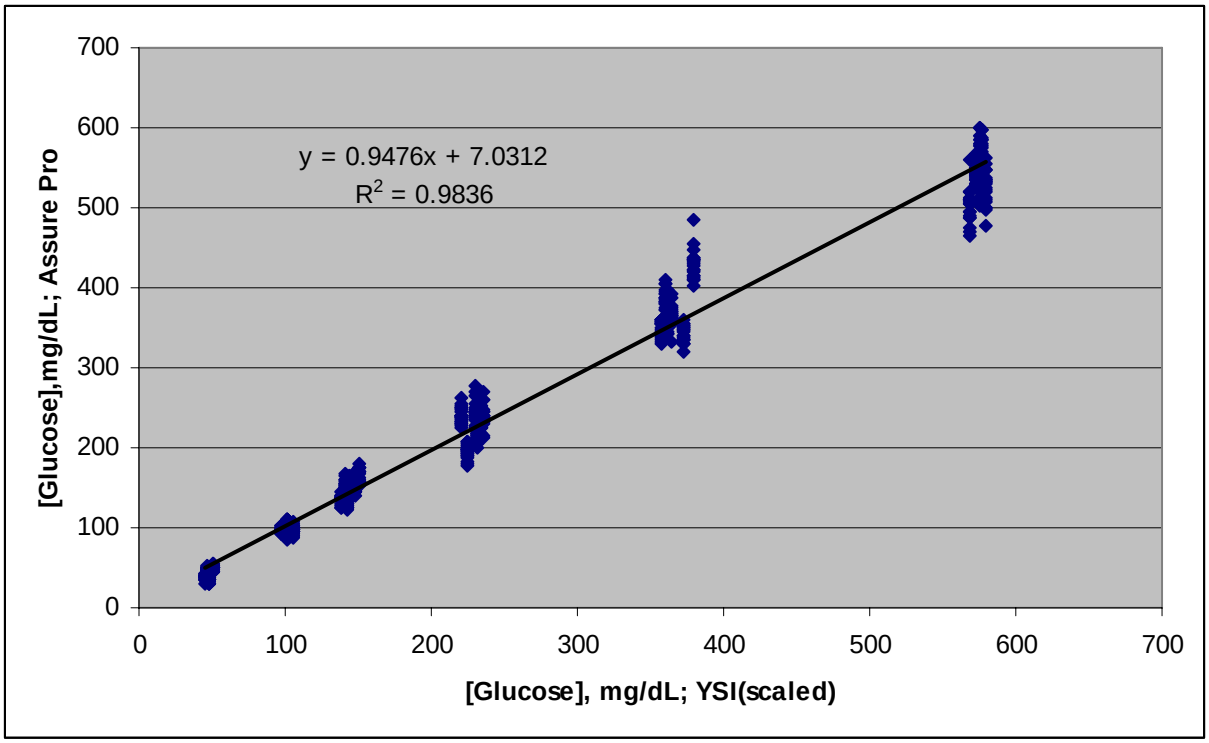
Mean Glucose Level (mg/dL)	*n*	*SD (mg/dL)*	*CV%*
46	296	2.8	6.1
105	300	4.1	4.0
138	299	5.4	4.0
231	300	9.2	4.0
348	300	16.0	4.6

b. Linearity/assay reportable range:

The company followed ISO 15197 and CLSI EP05-A2 in quantifying the precision of the linearity of their glucose system. The company collected 720 individual glucose measurements over 7 days. The company prepared a total of 36 separate glucose samples using spiked venous whole blood. Each glucose concentration was measured 20 times on a particular day. Blood was re-oxygenated before measurement. The company selected their glucose concentrations to meet IS 15197 sampling recommendations and to

span the full range of their device.

The following graph illustrates the linear relationship between the proposed device and a laboratory reference method.



A summary of the proposed device's ISO 15197 performance:

Glucose Concentration Range (mg/dL)	Number of Measurements outside ISO 15197	Weighted Percentage Error
0 – 50	5	0.25
50 – 80	0	0
80 – 120	0	0
120 – 200	0	0
200 – 300	2	0.25
300 – 400	1	0.083
400 – 1200	0	0
Total Weighted Percent Error		0.583

The information supplied by the company substantiates their claim for linear performance over the 20 – 600 mg/dL glucose concentration range claimed for this device. The information supplied by the company demonstrates that they meet ISO 15197 expectations for linearity.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The company used accelerated aging further substantiated by comparison to the storage behavior of their predicate device to determine the shelf life of their device. Three manufacturing lots of meter strips were stored at 45°C, 50°C, 60°C, and 70°C. Sets of 36 strips were periodically withdrawn from environmental storage and used for measurements. For each time point, the company made 6 replicate measurements at 6 different glucose concentrations spanning the claimed range of their device. The company used a 20% change in behavior as a criterion for determining when a strip was over-aged.

From their accelerated aging studies, the company concluded that the shelf life of their measurement strips was at least 36 months when stored at 30 °C. The company noted that the a comparative aging study of the new and predicate measurement strips indicated the proposed device demonstrated a factor of 3 greater shelf life when compared to the predicate. The predicate device has a shelf life of 21 months as confirmed by real-time studies.

The data supplied by the company supports the room temperature shelf life of 21 months claimed for the proposed device.

Control solutions for this device were cleared previously in the predicate.

d. Detection limit:

The company demonstrated the performance of their device near their high glucose limit using 2 test suites. Below the 600 mg/dL limit for the device, the company performed measurements on glucose enriched venous blood with glucose ranging from 573 mg/dL to 580 mg/dL as determined by a plasma YSI measurement. 88.8% of the measurements fell within 10% of the plasma YSI reference. 100% of the measurements fell within 20% of the plasma YSI reference. There were no non-numeric "HI" results.

The company challenged 8 meters with venous blood enriched to a glucose concentration of 698 mg/dL as determined by a YSI. All meters reported a "HI" reading instead of a numeric value.

The company validated the performance of their device at their low glucose limit using 2 test suites. In the first, the company challenged the performance of 8 production meters and 1 lot of strips using venous blood depleted to a glucose concentration of 6 mg/dL as determined by a plasma YSI reading. All meters reported a "LO" concentration.

The company further validated the performance of their device at low glucose concentrations using a meter whose software reporting limit was disabled for the test. The company made 32 measurements distributed evenly over 4 lots of strips with venous blood adjusted to a glucose of 21.7 mg/dL as determined by a YSI. They made an additional 8 measurements using an additional lot of strips (5 lots total)

using blood adjusted to a glucose concentration of 23.4 mg/dL. Of these 40 measurements, one point or 2.5% fell outside the ± 15 mg/dL range specified by ISO 15197. 11 of 40 measurements or 27.5% would have yielded numerical results to the user. All 11 of these numeric results were within IS 15197 limits.

The data provided by the company substantiates their claims for performance at the lower and upper limit, 20 mg/dL and 600 mg/dL respectively, and the measuring range of their device.

e. Analytical specificity:

Impact of Chemical Interference

The company assessed the impact of endogenous and exogenous chemicals on the performance of their device. The company followed CLSI EP07-A2 "Interference Testing in Clinical Chemistry" in assessing the impact of analytes on their device. The company used 3 lots of strips to measure the impact of added analytes at 2 different glucose concentrations: 70 mg/dL and 240 mg/dL. Chemicals tested for interference were added by spiking. The company used ISO 15197 guidelines as a limit for assessing interference. Additives that altered the devices response by more than 15 mg/dL for the 70 mg/dL solution or by more than 20% (48 mg/dL) for the 240 mg/dL were found to interfere.

A summary of the company's findings:

Analyte	Concentration (mg/dL)	Low Glucose Bias (mg/dL)	High Glucose Bias (mg/dL)	Interference
4-Acetamidophenol	15	36.3	45.84	Present
Acetylsalicylate	50	-0.8	-5.04	None
Ascorbic	3	14.8	22.56	None
Bilirubin (unconjugated)	12	10.5	11.28	None
Bilirubin (conjugated)	40	1.6	3.84	None
Cholesterol	500	-12.5	2.616	None
Creatinine	30	-4.7	-8.88	None
l-Dopa	3.4	33.6	26.16	Present
Dopamine	2.2	20.1	91.2	Present
EDTA	1600	4.3	-6.96	None
Ephedrine	1.1	-1.2	-3.84	None
Fructose	60	-1.1	-9.84	None
Galactose	60	-1.9	0.24	None
Gentisic acid	10	21	29.76	Present
Glutathione	2	-0.6	22.08	None
Hemoglobin	500	-2.4	-8.4	None
Heparin	10000	2.0	5.76	None
Ibuprofen	40	-6.9	-12.48	None

Analyte	Concentration (mg/dL)	Low Glucose Bias (mg/dL)	High Glucose Bias (mg/dL)	Interference
Lactose	60.0	-9.9	-1.68	None
Maltose	450	1.8	-7.44	None
Mannitol	800	-1.8	6.72	None
Mannose	26	-7.0	-9.84	None
Methyl-L-DOPA	2.5	-6.6	16.32	None
Salicylic acid	50	-6.0	-1.2	None
Sodium citrate	1000	0.0	15.84	None
Sodium fluoride	1000	2.1	6.72	None
Sodium oxalate	800	-5.6	11.28	None
Sorbitol	310	2.6	10.32	None
Tetracycline	4	1.7	10.08	None
Tolazamide	30	32.1	14.5	Present
Tolbutamide	100	-1.7	-1.2	None
Triglycerides	3000	-5.2	6	None
Urea	500	-0.7	-12.48	None
Uric acid*	6.8	20.7	-22.8	Present
Warfarin	10	1.3	-5.52	None
Xylitol	0.2	-4.2	3.12	None
Xylose	600	3.5	10.32	None

*Tests for interference data with uric acid were done with glucose solutions of 88 mg/dL and 225 mg/dL.

The company added statements to their product insert cautioning users against using this device when the interfering analytes might be present.

The company assessed the impact of maltose, maltotriose and maltotetraose in a separate test suite involving 3 different glucose concentrations tested over 10 meters. The company used venous blood spiked to the target glucose concentration. Glucose concentrations were confirmed through measurement on two separate YSI instruments. A summary of the company's findings:

Reference [glucose], mg/dL	Meter Reading, [maltose] = 0.0 mg/dL	Meter Reading, [maltose] = 120.0 mg/dL	Bias from Control
80 mg/dL	85.8	86.4	0.7%
150 mg/dL	181.8	187.8	3.3%
300 mg/dL	373.0	363.2	-2.6%

Reference [glucose], mg/dL	Meter Reading, [Maltotriose] = 0.0 mg/dL	Meter Reading, [Maltotriose] = 120.0 mg/dL	Bias from Control
80 mg/dL	89.9	87.4	-2.8%
150 mg/dL	190.5	187.4	-1.6%
300 mg/dL	373.7	360.6	-3.5%

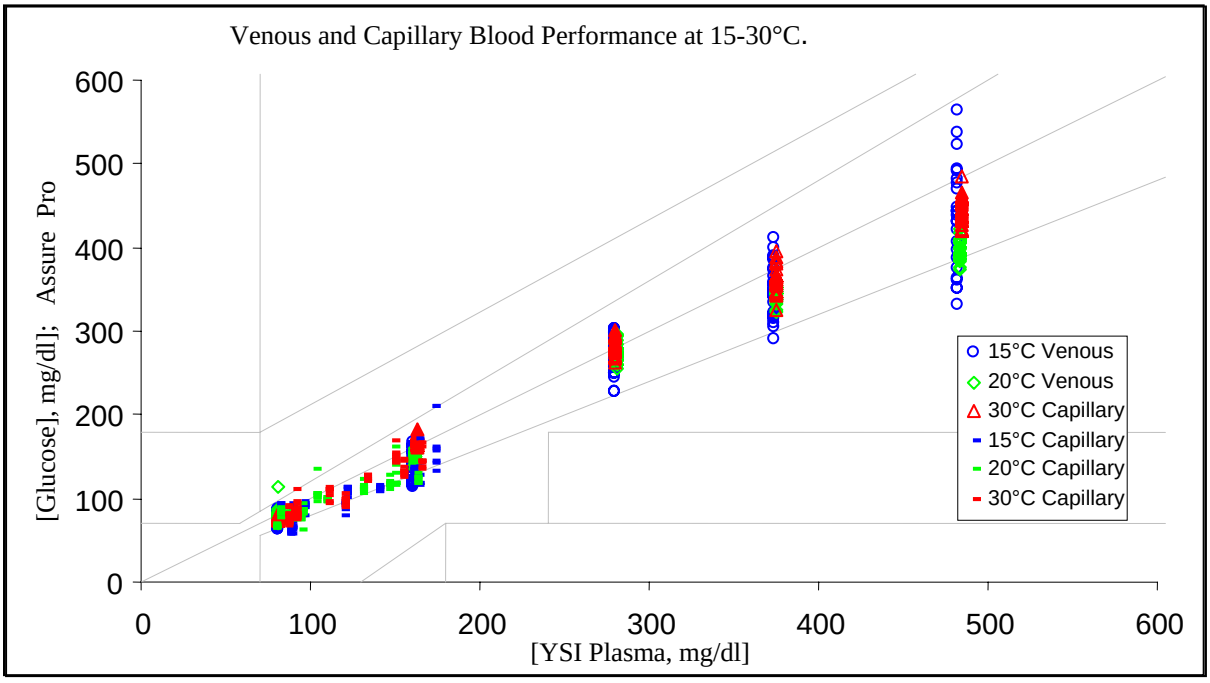
Reference [glucose], mg/dL	Meter Reading, [Maltotetraose] = 0.0 mg/dL	Meter Reading, [Maltotetraose] = 60.0 mg/dL	Bias from Control
80 mg/dL	88.3	86.2	-2.4%
150 mg/dL	188.8	185.4	-1.8%
300 mg/dL	352.6	361.1	2.4%

The data supplied by the company supports their claim that metabolites of icodextrin (maltose, maltotriose and maltotetraose) do not significantly impact the performance of the meter.

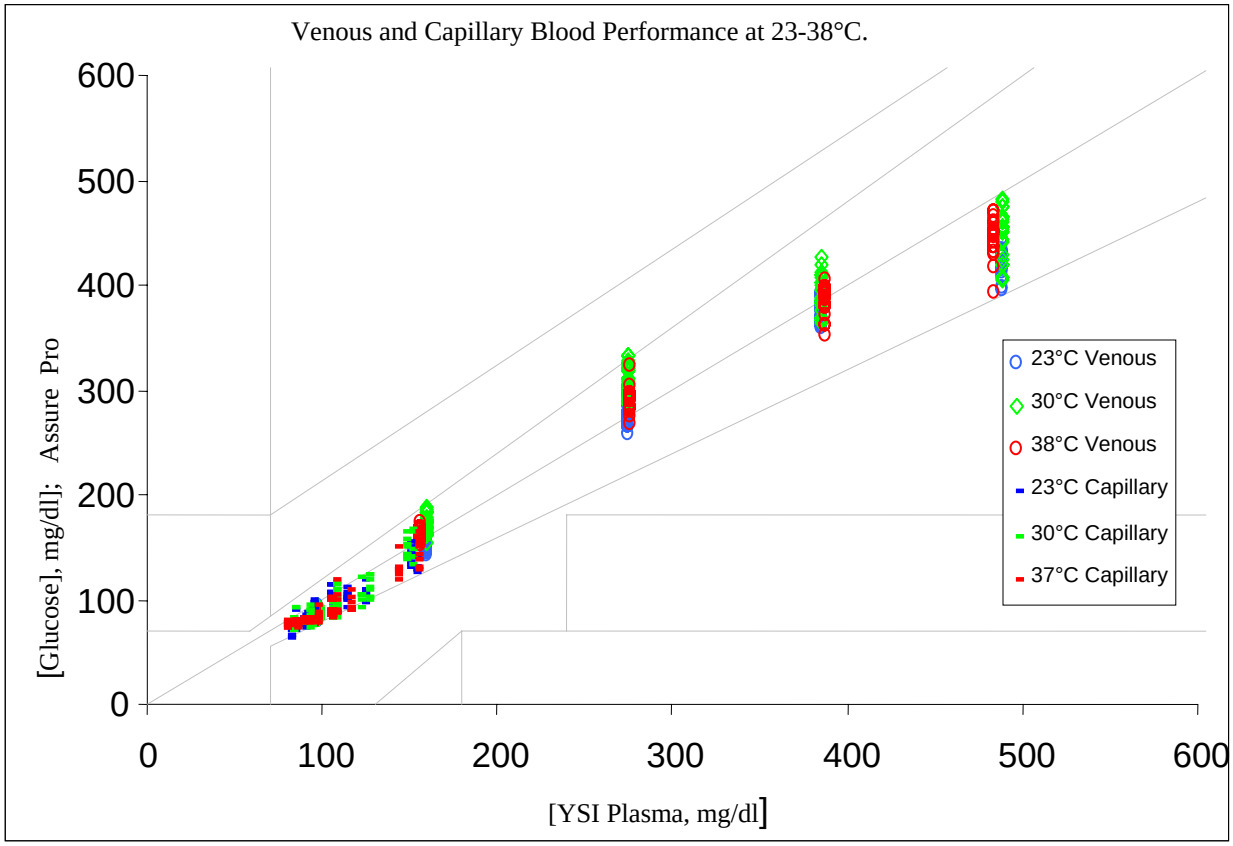
Impact of Temperature on Meter Performance

The company assessed the impact of temperature on their device in the measurement of venous and capillary blood. Venous blood was allowed to equilibrate in an environmental chamber prior to measurement. Capillary blood was applied as a hanging droplet and was assumed to have reached the target temperature before measurement.

The following graph illustrates the impact of temperature ranging from 15-30 °C on measurements made with this device:



The following graph illustrates the impact of temperature ranging from 23-38 °C on measurements made with this device:



The company opted to limit their claimed temperature range to 15 – 35 °C.

The data supplied by the company supports the claimed operating temperature range for this device.

Impact of Hematocrit

The company used fresh venous blood from non-diabetic volunteers to assess the impact of variations in hematocrit on the device. Concentrations of glucose were adjusted by spiking. Hematocrit levels were adjusted across the 30-55% range via centrifugation and re-suspension of the packed cells. Measurements were made on 7 different meters and across 4 lots of strips.

Using a total of 238 measurements, the company determined that in a glucose range of 74 – 121 mg/dL, variations in hematocrit introduced a linear change in their device's response that could be described by a line: Bias = -1.52 (%Hematocrit) +65.7. This met the company's acceptance criteria of bias less than ±20% across the claimed range for the device, 30%-55% hematocrit.

Using a total of 259 measurements, the company determined that in a glucose range of 411 – 466 mg/dL, variations in hematocrit introduced a linear change in their device's response: Bias = -1.27 (%Hematocrit) + 55.0. This met the company's acceptance criteria of bias less than ±20% across the claimed range for the device, 30%-55%

hematocrit.

f. Assay cut-off:

Not applicable to a device of this type.

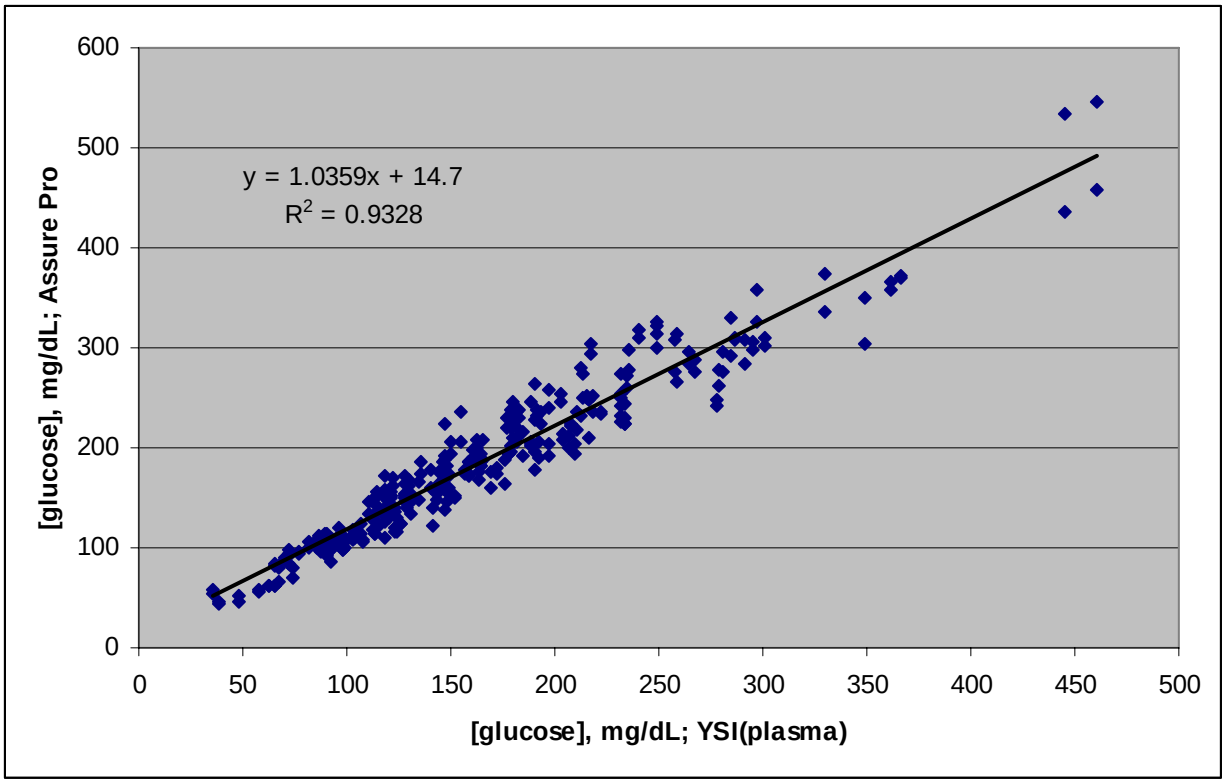
2. Comparison studies:

a. Method comparison with predicate device:

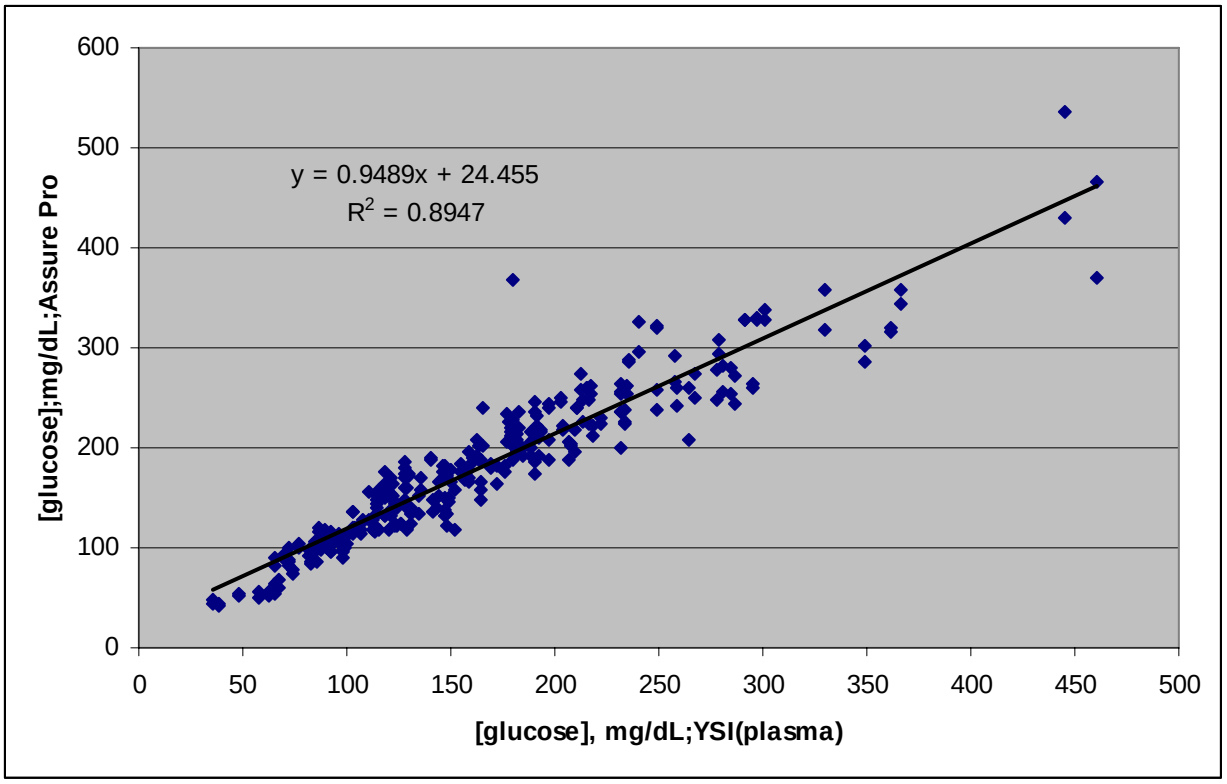
The company conducted a user study to assess the ability of diabetics to obtain a valid measurement with the device. The company recruited 159 diabetics to participate in the study. Evaluation subjects included both men and women, with Type 1, Type 2 or gestational diabetes, and ranged in age from sixteen to seventy-eight. Blood glucose concentrations ranged from 38.9 mg/dL to 498.1 mg/dL as determined by measurement with calibrated YSI, the device used as the reference method. Patients were provide with the instructions and training material that will be packaged with the for-sale product Study participants received no additional training, instruction, assistance or training material other than that packaged with the system.

Lay user participants made 2 sequential measurements with 2 different meters. Following the self-administered measurements, a physician performed a second set of 2 measurements with the two meters. 2 meters and 3 lots of strips were used in the study.

The following graph illustrates the performance of device when used by a physician as compared to a laboratory reference:



The following graph illustrates the performance of device when used by a lay user as compared to a laboratory reference:



b. Matrix comparison:

Not applicable to a device of this type.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable for a device of this type.

b. Clinical specificity:

Not applicable for a device of this type.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable for a device of this type.

4. Clinical cut-off:

Not applicable for a device of this type.

5. Expected values/Reference range:

The company cited the American Diabetes Association[1] for their reference values:
Fasting glucose concentrations: 90-130 mg/dL
2 hours after any meal: < 180 mg/dL
Bedtime: 110-150 mg/dL

[1]American Diabetes Association Web Page, 01/2004

N. Instrument Name:

Assure Pro Glucose Monitoring System

O. System Descriptions:

1. Modes of Operation:

   Test strips can only be used once. Users must replace the strip before taking an additional reading.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __Y____ or No _____

3. Specimen Identification:
   There is no sample identification function with this device. Samples are applied directly to the test strip as they are collected.

4. Specimen Sampling and Handling:
   This device is intended for use with fresh capillary whole blood. Since the sample is applied directly to the test strip, there are no special handling or storage issues.

5. Calibration:
   Each bottle of test strips is accompanied by an electronic key which contains information necessary to customize the performance of the meter to each lot of strips. The user changes the key on opening a new vial of test strips. The user has the option of comparing the code number for the key against the code number printed on the vial either through the user interface of the meter or by comparing the number printed on the key. No further calibration is required of the user.

6. Quality Control:
   The company provides two levels of glucose control solutions with this device. To perform a test on a control solution, the user first inserts a test strip into the meter's receptacle for strips. After confirming that the displayed numeric code matches the code for the key printed on the strip vial, the user presses the navigation keys until they enter

the control solution mode. This mode prevents the meter from automatically storing the results of the measurement of the control. The user then measures the glucose concentration of the control solution as described in the user manual. The user compares the output of this measurement to the acceptable range of measurements for each control level printed on the label of the test strip vial. If control results fall outside these ranges, the user is referred to a list of troubleshooting steps and the customer care line.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

The meter supports memory for storing 250 measurements. Once stored in memory, measurement values are independent of the calibration key currently loaded in the meter. When the memory of the device is full, additional measurements automatically overwrite the oldest stored reading. Saved results are stored with the date of the measurement and a number, e.g. 1,2,3 … , indicating the "n^{th}" measurement of the day. In addition, the meter supports a 7, 14, and 30 day moving average calculation for glucose concentrations. The device provides audible alarms to alert the user to low glucose measurements and to remind users to monitor their glucose.

Information on software and device testing provided by the company support their performance claims for this feature.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports substantial equivalence decision.